REMARKS

The Examiner found no prior art for the elected species and, accordingly, the Examiner searched for prior art that meets the limitations set forth in general formula I, as broadly claimed in claim 1.

The Claim Amendments

Applicants have amended claims 1 and 17 solely for the purpose of clarification. The amendments do not narrow the scope of the claims.

Applicants have amended claim 1 to recite the possibility that "X is a substituted aromatic compound with three functional groupings W_1, Y_1, Z_1, wherein W, Y or Z and W_1, Y_1, Z_1 are the same or different and selected from CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH2." This amendment is supported by the specification generally. See, for example, page 5 and the claims as originally filed.

Claims 1 and 17 are also amended to restore the variable "l" (lower case "L") in the structural formula. The "l" had been inadvertently replaced with an "I". In order to prevent future confusion in this regard, we have replaced the "l" (lower case "L") with a cursive "ℓ". This amendment is supported, for example, by claim 1 as originally filed.

The amendments do not introduce new matter.

Priority Documents

The Examiner acknowledges applicants' claim for foreign priority, but notes that certified copies of the priority documents have not been filed.

Applicants are filing certified copies of the priority documents with this response.

The Rejections

35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1 – 14, 16, and 17 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner contends that the recitation "$W_1Y_1Z_1$" in part (iv) of claim 1 is unclear. The Examiner states that "$W_1Y_1Z_1$" is not described in the disclosure and it is unclear whether these are the same as W, Y, and Z from general formula I.

The Examiner further states that it is unclear whether "l" in the last line of claim 1 is intended to be an "I," which is used in general formula I. The Examiner indicates that this renders indefinite the recitation in claim 17 of "the combination of claim 1, wherein I is 1." We propose to amend the claim to clarify that the variable should be "l."

Claim 1 has been amended solely for the purpose of clarification. The element "$W_1Y_1Z_1$" is amended to read "W_1, Y_1, Z_1" wherein W_1, Y_1, and Z_1 may be selected from among the same moieties as W, Y and Z.

Claim 1 is further amended to change the "I" in the representation of the formula back to an "ℓ" (a lower case "L"). Claim 1 as originally filed listed a lower case "l", not an "I" at this position. The "ℓ" of the formula in the amended claim corresponds with the "ℓ" in the last line of the claim, thus obviating the rejection.

35 U.S.C. § 102(b), Novelty

The Examiner has rejected claims 1 – 9, 12 – 14, 16, and 17 under 35 U.S.C. § 102(b) as allegedly anticipated by WO 98/19710 ("Schacht"), which was cited in the Information Disclosure Statement. Specifically, the Examiner alleges that when m and n are 0, the general formula I encompasses compounds that belong to the general formula R-W-X-Y (variable "l" must also be 1), wherein R is an amphiphilic polymer or derivative thereof, W and Y are CO, NH, O, S, or a linker capable of reacting with SH, OH, CH, or NH_2. Applicants traverse.

In order to anticipate the present claims, Schacht must teach or inherently embody all of the elements of the claims. Schacht omits various elements of the present claims.

The pending claims recite (1) a carrier, (2) a nucleic acid molecule, and (3) a charged copolymer. Dependent claim 6 further recites that the nucleic acid is complexed with an organic polycation or cationic lipid.

Schacht only discloses complexes comprising (1) a nucleic acid molecule, (2) a charged copolymer and (3) a hydrophilic polymer. Thus, Schacht does not teach the additional feature of a carrier. Schacht does use the term "carrier", but with a different meaning than the present application.

Schacht uses the term "carrier" to refer to the nucleic acid-containing complexes as a whole, and not in reference to any particular component of the complex. For example, Schacht writes:

> [T]he invention provides a nucleic acid carrier vehicle for delivery of nucleic acid material to target cells...said carrier vehicle being in the form of a polyelectrolyte complex comprising a nucleic acid-containing cationic polymer core associated with hydrophilic polymer material that forms an outer stabilizing steric shield or coating. (p. 4, lns. 3-9.)

In claim 48, Schacht recites:

> [A] synthetic polymer-based carrier vehicle *that comprises* a polyectrolyte complex in which a plasmid DNA expression vector...is condensed...with a polycationic polymer...that is coupled...to associated hydrophilic polymer material that provides a stabilizing steric shield around the complex. (*emphasis added.*) (p. 58, lns. 20-26.)

Therefore, Schacht does not use the term "carrier" to refer to a particular element of the nucleic acid-containing complexes. Schacht uses the term to refer to the complexes as a whole. The Examiner cites page 12, lines 8-11 as allegedly teaching the use of polyhydroxymethacrylamide (pHPMA) as a "carrier". In fact, this passage refers to pHPMA as "one preferred category of polymeric material for providing the hydrophilic polymer components of the complexes of this invention." Thus, Schacht refers to pHPMA not as a carrier itself but as a hydrophilic polymer which is a component of the carrier as a whole. Furthermore, Schacht

does not teach any other component of these complexes that would fulfill the role of the "carrier" as described in the present application.

The present application refers to a carrier as, "a body or a substance which can be contacted in vivo or in vitro with cells to be transformed and which carries the complex of nucleic acid(s) and copolymer(s)." (p. 18, lns. 6-8.) Specific examples of carriers provided in the specification include, without limitation, sponges, powders, gels foils, etc.

Because Schacht does not teach or suggest any element corresponding to a carrier, Schacht does not anticipate the pending claims.

Applicants request reconsideration and withdrawal of this rejection under 35 U.S.C. 102(b).

35 U.S.C. § 103(a), Obviousness

The Examiner has rejected claims 1 and 9 – 11 under 35 U.S.C. § 103(a) as allegedly unpatentable over Schacht in view of United States Patent 5,863,984 (Doillon). The Examiner contends that Schacht teaches a combination of a carrier complex comprising a therapeutic nucleic acid molecule and a charged copolymer that meets the structural limitations of the claim. The Examiner acknowledges that Schacht does not teach that the carrier is a collagen sponge. The Examiner states that Doillon teaches a PEG-modified collagen sponge that can be used as a drug carrier. The Examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to modify the complex of Schacht such that the complex was comprised an a collagen sponge such as the one taught by Doillon. Applicants traverse.

One of ordinary skill in the art would not be motivated to combine the polymer-nucleic acid complexes of Schacht with the carriers of Doillon. Schacht does not describe any carriers at all, and nor does Schacht suggest that a material with carrier-like properties would be useful in the delivery of nucleic acids. Doillon does discuss collagen sponges, but provides no motivation for the use of such sponges in association with polymer-nucleic acid complexes.

Doillon is directed to the field of "porous material useful as wound scaffolds." (Col. 1, lns. 5-6.) Doillon cites a "need for sponges containing biopolymers capable of supporting cell growth which have a stabilized porosity, allowing for colonization of fibroblasts." (Col. 3, lns. 21-24.) Doillon satisfies this need by describing collagen sponges that are "impregnated with a solution of PEG derivatives and allowed to react therewith to obtain composite matrices which have stable porosity." (Col. 4, lns. 45-47.) Thus, Doillon is concerned with the preparation of collagen sponges that have a stabilized porous structure so that cells can colonize the sponge in the setting of a wound. Doillon does not suggest the use of collagen sponges for the delivery of nucleic acid complexes.

The Examiner cites the following passage from Doillon:

> Thus, the stability of the PEG-modified collagen sponges might be linked to the repulsive properties of PEGs after which their covalent binding to the amino groups of the proteins stabilize the tertiary structure thereof. In addition, with *PEG-conjugated liposomes used as drug carriers, the repulsive barrier properties of lipid-conjugated PEG polymer chains and polymer steric stabilization are the basis for their extended in vivo circulation times. (emphasis added.) (col. 18, lns. 13-21.)*

Because of the statement above regarding increased in vivo circulation times, the Examiner suggests that this passage would motivate one of ordinary skill in the art to use pegylated collagen sponges in the delivery of nucleic acids. However, this passage only discusses increased circulation times with respect to PEG-conjugated liposomes. The paragraph does not suggest that pegylated collagen sponges should be used for drug delivery. The cited passage is excerpted from a larger paragraph that describes the advantages of the pegylated collagen sponges. These advantages are described by comparison to the effects of pegylation on the behavior of liposomes. While pegylated liposomes are known and used for drug delivery, the paragraph does not suggest that pegylated or non-pegylated sponges should be used for drug delivery, nor does the paragraph suggest that collagen sponges should be used for any purpose other than the central goal Doillon, which, as described above, is to provide a material for colonization by cells in wound repair.

Therefore, Doillon provides no motivation to the skilled artisan to use collagen sponges for the delivery of nucleic acids to cells, and therefore no motivation to combine the teachings of Doillon and Schacht.

For these reasons, Applicants request withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

For the reasons presented above, Applicant requests that the Examiner allow the claims, as amended, to issue. The Examiner may address any questions raised by this submission to the undersigned at 212-596-9000. Applicant hereby requests that any fee required, in addition to the fee supplied with the Request for Extension of Time, be charged to Deposit Account No. 06-1075.

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Respectfully submitted,

By _____

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